

make a diagnosis at times between ulcer and cholecystitis. I believe that in these cases we should say as do the Mayos very frequently: "You have a surgical condition in the upper right quadrant of your abdomen, and you will have to be satisfied with that diagnosis." I have seen recently four cases, one right after the other, in which adhesions were found between duodenum and colon or duodenum and gall-bladder without any signs of previous ulceration.

Dr. G. E. Ebricht: I shall confine myself to one point: the treatment of hemorrhage. In cases of hemorrhage the mortality in cases left alone is in the neighborhood of two per cent. It requires rare judgment and rare courage, in considering a patient who has severe bleeding from stomach ulcer, to realize that if let alone his chances are better than when interference takes place. As the blood is lost, the blood pressure is lowered to such a point that clotting may take place, and the bleeding gradually stops. For that reason we avoid using cardiac stimulants in shock just as much as possible. The use of adrenalin and drugs of that nature is much best left alone if possible. If styptics can be applied locally to the bleeding point, it is a different thing, but agencies to raise the blood pressure and stimulate the patient out of shock, should be used with extreme caution.

Dr. L. Eloesser, closing discussion: We have been fortunate with our results at the City and County Hospital, more fortunate than Dr. Schmoll would indicate. We have had about a dozen cases, treated by gastro-enterostomy, resection and excision, and have been lucky enough to have had them all recover. I think it has been due in great measure to Dr. Hill's help. We have tried to work with the physician, rather than against him, and have consulted and respected his opinion as to indications for operation.

If we cannot cure causes of ulceration, medical men cannot cure them either. Perhaps we can, however, do more to cure the causes of ulceration than medical men by treating, when we open the belly, concomitant conditions, by removing the appendix or the gall-bladder.

I must strongly protest against Dr. Bine's dictum that the hour-glass stomach is not a subject for surgical intervention. I should like to ask what he means by an hour-glass stomach. Dr. Alvarez says that the hour-glass stomach disappears at operation—that it disappears under an anesthetic. Now, a true hour-glass stomach does not disappear under the anesthetic at all. Those cases that disappear are not hour-glass stomachs; they are spastic stomachs, X-ray stomachs, if you like. You can diagnose them. If the X-ray shows an apparent hour-glass, give the man a physiological dose of atropin and X-ray him again. If the spasm is gone, he has no hour-glass stomach. If you operate for hour-glass stomach and he really has one, it will not disappear under ether. You will see a scar and a constriction so firm, inelastic and tight at times that you cannot get a finger into the opening.

As to bleeding, I think, too, that bleeding in acute ulcer is not a case for surgical intervention. In aged individuals, however, when the arteries are hardened, it does not stop unless you close the vessel surgically. In acute ulcers, bleeding stops because the vessel is not sclerotic and can close by itself. These cases are for medical treatment.

I have not gone into the various surgical procedures, because I thought that their discussion was more for a surgical than a medical meeting. I think the Finney operation is valuable in many cases of pylorospasm; it does away with the dangers of vicious circle. The use of the Finney in duodenal ulcer, I think is not as good as gastro-enterostomy—we get too close to the ulcer itself, for one thing, and we do not get the reflux of alkaline intestinal contents into the stomach for another.

THE DOSE OF SALVARSAN.

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Because of the occasional occurrence of encephalitis hemorrhagica and other accidents, the dose of salvarsan is undergoing decided modifications. The dose recommended for general use when the drug was first introduced was 0.60 grm. for males and 0.40 grm. for females, equivalent in neosalvarsan to 0.90 grm. for males and 0.60 grm. for females. When these doses are carefully given, in almost every instance they are borne without any disagreeable symptoms whatever. There may be some vomiting, there may be some diarrhea, there may be some diuresis, but the patients usually arise from the couch, on which they have received their infusion, and experience no ill effects. Deaths do, however, result from the administration of salvarsan, and they are particularly distressful. When such an accident occurs quickly following the infusion of a drug into the blood, the physician cannot escape the feeling of responsibility, nor can he elude the censure of those that surround him. Both remorse and blame are especially sharp in those instances in which the medical man has strongly urged the acceptance of the treatment. As the whole dose is administered intravenously and at one time, it is therefore irretrievable, and when once given it goes on its way for good or for evil without any essential modification of its action being possible.

Barring accidents from faulty technique or from disability on the part of the patient, such as a persistent status thymo-lymphaticus, advanced disease of the liver of the kidneys or illy compensated valvular disease with cardiac myodegeneration, the accidents from salvarsan are very few indeed. Deaths, however, have occurred when the dose was moderate, when there was every reason to suppose the drug was unchanged, and when the technique was faultless, and when the patient seemed in every respect suited to receive the treatment. It would seem that in these rare cases the patients are abnormally susceptible to the drug. This hypersensitiveness to salvarsan may involve the skin, the gastro-intestinal tract, the kidneys, the liver or the brain and its meninges. This last class of cases in which the brain and its meninges are hypersensitive to salvarsan, constitutes by far the most interesting group.

Meirowsky and Kretzmer have tabulated the deaths from salvarsan, and these tabulations are most impressive in their bearing on the dosage, and on the question of encephalitis hemorrhagica.¹ In all there are only one hundred and nine deaths. As far over a million doses had been given when these tabulations were made, and as a multitude of causes, besides the nature of the drug itself, entered into the result, the small number of fatalities is remarkable. And this small number cannot be ascribed to inadvertence in reporting cases, as no drug has been watched half so jealously as salvarsan.

In eighty-five cases the stage of syphilis at which the death occurred is noted. It appears that in twelve of them the dose was given and the death

occurred when the patients were in the primary stage of syphilis; in thirty-five when they were in the secondary stage, and in seven when they were in the tertiary stage. In eight of these fatalities the patients had latent syphilis, and in twenty-three, the patients had syphilis of the central nervous system, such as tabes, paralysis or cerebral lues.

These figures are surprising indeed as they show such a large percentage of the deaths, thirty-five out of eighty-five cases, or 41.2%, in secondary syphilis. This heavy death rate in secondary syphilis is brought out still more saliently if only the cases of encephalitis hemorrhagica are considered.

CASES OF ENCEPHALITIS HEMORRHAGICA CLASSIFIED ACCORDING TO THE STAGE OF THE DISEASE IN WHICH THE ACCIDENT OCCURRED.

Meirowsky and Kretzmer have collected thirty-four of these cases. In six of them death occurred in the primary stage of syphilis, seventeen in the secondary stage, and two in the tertiary stage. In five of the cases the patients had latent syphilis, and in four the patients were suffering from some form of syphilis of the central nervous system, such as tabes, paralysis or cerebral lues.

In this last enumeration, seventeen, constituting 50 per cent. of the deaths occurred in patients suffering from secondary syphilis. Clearly those in the secondary stage of syphilis show a greater susceptibility to a disastrous result, and to a disastrous result involving the cerebrum, than those in any other stage of syphilis.

The susceptibility of those in the secondary stage of syphilis to this particular kind of accident stands out still more prominently when one reflects that the acquisition of syphilis is most frequent at the height of sexual development and therefore in individuals in the prime of life and health, and that the secondary period follows close on the primary stage, or stage of acquisition, and therefore with individuals equally robust. The accident, therefore, is not due to constitutional weakness in the individual, as those, for instance, suffering from syphilis of the central nervous system must be constitutionally much weaker. Nor is it true that the total number of treatments during the secondary stage equals or exceeds the treatments in all the other stages combined; on the contrary the treatments during the other stages must by far exceed those in the secondary stage.

Tomasczewski believes that the accidents attributable exclusively to salvarsan are due to ideosensitiveness; in one case affecting the skin and giving rise to a Herxheimer reaction, in another affecting the kidneys, in another reacting on the gastro-intestinal tract, in another affecting the liver and in still others producing a meningeal and cerebral symptom-complex. It is thought that the presence of any septicemia, whether spirochetal or other, may peculiarly sensitize the brain and meninges, and so account for the comparatively large number of instances of encephalitis hemorrhagica occurring during the secondary stage of

syphilis, in which a spirochetemia undoubtedly exists.

THE NUMBER OF DOSES AND THEIR SIZE, AND, IF MORE THAN ONE DOSE IS ADMINISTERED, THE PROXIMITY OF THE DOSES, AS CONTRIBUTING TO A FATAL RESULT.

Cases in which death occurred after one dose:

In thirty-six cases there were three fatalities after one dose of 0.30 grm. or less; six fatalities after one dose of 0.31-0.40 grm.; eleven fatalities after one dose of 0.41-0.50 grm. and sixteen fatalities after one dose of 0.51 grm. and over.

Cases in which death occurred after two or more doses of salvarsan:

There are forty-five fatalities in this category. Only the size of the last dose is here considered. In the forty-five cases, one death occurred after a final dose of 0.20 grm. There were six fatalities after a final dose of 0.21 to 0.30 grm.; ten fatalities with a dose of 0.31 to 0.40 grm.; ten fatalities with a dose of 0.41-0.50 grm.; and eighteen fatalities with a dose of 0.51 grm. and more.

Another very interesting table takes under consideration the size of the dose and the fatalities from encephalitis hemorrhagica. There are in all forty-one of these cases, and there was one fatality at a dose running from 0.20-0.29 grm.; five fatalities at a dose running from 0.30-0.39 grm.; eight fatalities at a dose running from 0.40-0.49 grm.; and twenty-seven fatalities at a dose of 0.50 grm. and over. It will be seen that the fatalities increased with the dose, and that twenty-seven or 65.8% of them occurred when the dose was 0.50 grm. or more. However, it will also be noted that although the larger the dose the more apt encephalitis hemorrhagica is to occur, yet it may supervene even on the administration of a very moderate dose, 0.30 grm. or less. Furthermore, its supervention cannot be ascribed to any fault in technic or to any change in the drug, but is a poisonous manifestation of salvarsan itself.

RELATIONSHIP OF THE DEATHS TO THE REPETITION OF THE DOSE.

It would appear that when the dose is repeated within a week the danger from salvarsan is much increased. In thirty-six cases when a second dose was given and death followed, twenty, or more than half of them, occurred when the second dose was given within a week from the first, and seven occurred when the dose was repeated within two weeks.

Meirowsky and Kretzmer conclude from all the facts they have been able to gather that the size of the dose and the intervals between doses are the two decisive considerations, and they propose to make it a principle never under any circumstances to give more than from 0.30 grm. to 0.40 grm. of salvarsan to a dose, and never to repeat the dose before the lapse of eight to fourteen days. Taking the number of injections of salvarsan at a million and the number of deaths at a dose of 0.30 grm. of salvarsan at ten this would give a chance of one in one hundred thousand that a death would happen. But in subjecting these ten cases to a

critical analysis they find that a number of the deaths could have been avoided. One of the patients of this group had aortitis luetica with myodegeneratio cordis, and died of pneumonic embolus. Another of the patients had tonsillar swelling, high fever and icterus after a first injection of 0.40 grm., which were direct contraindications against giving the second dose, after which he died. Another of these patients was very fat, and suffered from mitral insufficiency. Coma set in thirty minutes after the injection that ended in death. At the autopsy both cardiac ventricles were markedly dilated, and there was oedema of the brain. Another patient at the time of injection was suffering from severe nephritis, which is an absolute contraindication for this treatment. Another died five weeks after the last injection, and therefore the connection between the death and the administration of the dose was improbable. Another got three doses of 0.30 grm. within thirteen days, and they were, therefore, too quickly repeated. Six out of the ten fatalities were evidently due either to weaknesses inherent in the patient, or to the dose being repeated when a contraindication like icterus was present, or to repeating several doses too quickly. With care, therefore, in employing this dose of 0.30 grm. the deaths might have been reduced to four in a million; a very low death rate indeed.

At a recent meeting of the Berlin Medical Society, E. Lesser stated that a sufficient and requisite course of treatment consists in giving three or four intravenous injections of 0.30 to 0.40 grm. each of salvarsan.² One such injection is given every two or three weeks, and mercury is administered in the intervals. This course would, therefore, take from six to nine weeks for its completion. E. Lesser is a man of the widest experience, and of most excellent judgment, and his recommendations in this matter are to be regarded with the utmost seriousness.

At the same meeting Friedlander advised a dose as low as 0.30 grm., even when the chancre was present. For later symptoms he recommended one dose of 0.30 grm. followed by smaller doses, so that the total amount given in a course of six weeks would be 1.50 grm. Bruns advised frequently repeated small doses, and remarked that of the eighty-seven cases of encephalitis hemorrhagica reported according to Mentberger in literature, fifty-seven had received a dose of over 0.30 grm., which was in his opinion too high. Rosenthal got his best results by employing mercury and two or three intravenous injections of 0.30 to 0.40 grm. of salvarsan each, and Isaac said that when the chancre was present he got constant abortive results by giving three or four doses of 0.30 grm. each.

I personally have been accustomed to give a much larger dose of salvarsan, 0.90 grm. of neosalvarsan, equivalent to 0.60 grm. of salvarsan, but the above statistics and expressions of clinical experience have modified this, because in the vast majority of instances, doses of 0.30 to 0.40 grm., when rightly managed, achieve everything that can

be accomplished by the drug, even to the definite extinction of the disease, and the larger dose can do no more than this, and exposes the patient to a risk that can be decidedly minimized by employing a smaller dose. Even in those cases of persistent Wassermann reaction, without the presence of any other symptom whatever, the best treatment seems to be repeated moderate doses of salvarsan with injections of grey oil intervening.

The above statistics of Meirowsky and Kretzmer must, however, have their most telling effect in our attitude towards patients in the early secondary stage of syphilis when the spirochetemia is at its height. Here either of two courses may be pursued. One small dose may be given to reduce the spirochetemia, followed by ordinary normal doses of 0.30 or 0.40 grm. of salvarsan combined with mercury. Instead of this a few doses of mercury may first be given as advised by E. Lesser. This would also reduce the spirochetemia, and would then permit the administration of ordinary doses of salvarsan.

In this review, for the sake of simplicity, the dosage of salvarsan has been given, and that of neosalvarsan rarely referred to. Neosalvarsan, however, in the relationship as marked on the tubes, is to be regarded as just as effective as salvarsan, is much easier of administration, and not nearly so toxic when by mischance it infiltrates into the tissues.

As regards a lower dose for women than for men, in my own experience I must say that women bear the same dose as men equally well. I think the idea of giving women a smaller dose of this drug rests on the laboratory practice of giving a dose according to the weight of the animal experimented upon. This may be a good rule as between the smaller and larger animals used in laboratories, but in such large beings as man the difference in weight between the male and the female cannot be of such importance. Of 109 cases of death from salvarsan, eighty-six were males and twenty-three were females.³ That is to say the deaths in males were three times greater than in females, but this difference rests probably on the greater number of males who have syphilis and who therefore have received treatment.

Personally, I should be inclined to consider all doses above 0.45 grm. as high and all below 0.25 as low, without, however, presuming to dictate that a higher dose than this shall not be given. The physician must be left free to use his judgment within very wide limits in the individual case. It is, however, required from him that he shall know the drug he is employing and that he shall have a clear idea of the results he wishes to obtain.

(1) Die Salvarsantherapie der Syphilis von Dr. Meirowsky und Dr. Kretzmer. Praktische Ergebnisse auf dem Gebiete der Haut- und Geschlechtskrankheiten. Edited by A. Jesionek. Dritte Jahrgang. 1914, S. 444.

(2) Berliner Medizinische Gesellschaft. Sessions of March 4 and 11, 1914. Original report by Drs. Felix Pinkus and O. Sprinz. Dermatologische Wochenschrift, May 9, 1914.

(3) Meirowsky and Kretzmer, loc. cit.